

October 21, 1999

VETERINARY SERVICES MEMORANDUM NO. 800.61

Subject: Split Manufacturing of Veterinary Biological Products

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics

I. PURPOSE

This memorandum provides guidance concerning veterinary biological products prepared under split manufacturing arrangements according to 9 CFR 114.3 (d).

II. CANCELLATION

This memorandum cancels Veterinary Services Memorandum No. 800.61, dated December 27, 1996.

III. BACKGROUND

Split manufacturing, which includes the production of licensed products for further manufacture, allows two or more producers to participate in the production of a licensed veterinary biological product for final use. The authority for allowing the production of veterinary biologics for further manufacture under split manufacturing arrangements appears in 9 CFR 114.3(d).

IV. DEFINITIONS

A. Split Manufacturing

Split manufacturing is an arrangement whereby two or more producers perform significant steps in production resulting in a product for final use.

B. Product for Further Manufacture (FFM)

An FFM is a partially prepared product or a serial of completed product that is meant to be used for producing another FFM product or a product for final use.

C. Final-use Product (FUP)

An FUP is a product in its final container meant for final use.

D. Significant Step in Production

For the purposes of this memorandum, a significant step in production is any step in the production of a biological product from the initiation of production with production seed up to and including the filling of the product (either liquid or dry) into final containers. Sampling, labeling, testing, and assembling final containers into a combination package are not considered significant steps in production.

V. **GUIDELINES**

A. Where to Split

The preparation of an FUP may be split after any significant step in production (except filling into final containers).

B. Number of Licensees

The number of licensees participating in the preparation of an FUP is not limited, provided that each licensee conduct at least one significant step in production.

C. Establishment License Requirement

Each firm participating in a split manufacturing arrangement must have an establishment license. A firm may qualify for an establishment license based on one or more products that qualify for a license for further manufacture or for final use.

D. Product License Requirement

Each firm participating in a split manufacturing arrangement must have the appropriate product license: an FFM license if the firm is performing beginning or intermediate steps; an FUP license if the firm is performing the final step(s); both of these licenses if the firm is performing beginning and/or intermediate step(s) in production, sending the FFM to another firm(s) for further steps, and then completing the FUP.

E. Data to Support Licensure

With regard to the overall data necessary to support licensure, an FUP produced by split manufacturing is no different from a similar product made by a single firm.

F. Product License Eligibility.

An FFM will not be licensed until it is incorporated into an FUP that qualifies for licensure. For a given FUP, CVB will issue all FFM licenses and the FUP license simultaneously. (Where the

FFM or FUP license already exists, this license will not be re-issued; however, the outline will need to be updated with the appropriate information.)

G. Outline of Production

An Outline of Production must be filed for each FFM and for each FUP. An FFM outline must identify the firm(s) authorized to receive the FFM and the conditions for shipment and receipt. The outline for any product that includes or incorporates one or more FFM's must identify each FFM supplier, each FFM product code, and the minimum specifications for acceptance.

H. Testing, Sampling, and Release of FFM's

Each FFM licensee is responsible for any testing indicated in part IV of the Outline of Production for that FFM. Each FFM licensee should collect and hold samples of its FFM serial(s). FFM serials must be released by the Center for Veterinary Biologics-Inspection and Compliance (CVB-IC) before they can be shipped to another licensee. Requests for release should include a completed APHIS Form 2008, with block 9 (TEST DATA) reporting only results of tests required in part V of the FFM Outline of Production.

I. Testing, Sampling, and Release of FUP's

Either the FUP licensee or the FFM licensee must test the serials of the final container product (or bulk completed product for nonviable liquid products). However, each FUP licensee must report the test results for its serial(s) to CVB-IC on a completed APHIS Form 2008. Each FUP licensee must also collect and hold samples of the FUP serial(s) produced and submit samples to the Center for Veterinary Biologics-Laboratory (CVB-L) prior to serial release. The Outline of Production for the FUP should indicate if a test in Part V of the outline is conducted by the FFM licensee.

J. APHIS Form 2008 Submitted by the FUP Licensee

The FUP licensee should provide the following information in block 11 (REMARKS) for each FFM licensee involved with this product: the FFM establishment license number, FFM product code number(s), and all FFM serial or subserial number(s). If necessary, include APHIS Form 2008A in order to list all FFM serial or subserial numbers.

K. Shipping and Shipping Conditions for FFM's

The Outline of Production for each FFM in a split manufacturing arrangement should indicate which firm(s) is (are) responsible for shipping between firms. The appropriate shipping conditions depend on the particular situation with consideration given to factors such as: stability of the product, time in transit, size and shape of containers, insulation of containers, and ambient temperature. The outlines prepared by the sending and receiving firms should agree concerning

clearly specified conditions and responsibility for shipping and receipt. Licensed FFM product may be shipped to the FUP firm in final containers that are unlabeled. Ship unlabeled final containers in sealed shipping boxes adequately identified as to contents with an approved FFM label.

L. Product True Names and Codes

Each FFM and each FUP must have its own true name and its own product code. The true name of an FFM describes only the FFM product itself and not the FUP into which it will be incorporated. The product code of an FFM begins with a letter; the product code of an FUP begins with a number. The source of the fractions or components of an FUP does not affect its true name or product code; an FUP produced by split manufacturing has the same true name and product code as a similar product made by a single firm.

M. Labeling

Each FFM and each FUP must have its own label (but see section K of this memorandum). The FUP must be labeled at the establishment holding the FUP license under which the product is being marketed. Requirements and guidelines concerning packaging and labeling appear in 9 CFR 112 and in VS Memorandum 800.54.

N. Combination Packages

All the final containers in a combination package should contain the name, establishment number, and serial identification of only the firm that assembles these final containers into the combination package. This firm must have performed at least one significant step in production for at least one of the final container components to be issued an FUP license for a combination package product.

O. FFM's for Export

The outline for an FFM for export must identify each country where the product is to be shipped and the facilities that will receive the product. The FFM producer should provide APHIS with evidence of the foreign country's approval for each product. APHIS does not require testing either by the firm or by CVB-L for an FFM product license for a product for export. If the FUP is licensed in the United States, the FFM producer needs to submit to APHIS a document from the importing country indicating that the authorities in the importing country know the nature of the FFM product. If the FUP is not licensed in the United States, the FFM producer needs to submit documentation from the importing country that the FUP is licensed (registered, authorized) in the importing country.

P. Imported FFM's

Imported FFM's must conform to the regulations in 9 CFR 104.5. The importer must obtain a permit for distribution and sale as indicated in 104.7. The FFM should also conform to the relevant points discussed in this memorandum.

Q. Records Retention for FFM's

The FFM licensee(s) should maintain records for a period of 6 years from the filling date of an FFM serial.

R. Sample Retention for FFM's and FUP's

It is required for FUP's and recommended for FFM's that reserve samples be selected and retained as indicated in 9 CFR 113.3(c).

S. Regulatory Action

If any FUP or FFM is found to be unsatisfactory according to an applicable Standard Requirement or Outline of Production, APHIS may notify all licensees in the particular split manufacturing arrangement to stop production, distribution, and sale of all the components, serials, subserials, and products in question.

/s/ Thomas E. Walton for

Alfonso Torres
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